UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/473,830	12/28/1999	JEFFREY M. LEIDEN	2844/53802	1518

28089 7590 09/24/2002

HALE AND DORR LLP
300 PARK AVENUE
NEW YORK, NY 10022

EXAMINER
CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/473,830	LEIDEN ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 7-8-02 has been entered. Claim 24 has been amended. Claims 24-46 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 24-46 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention and is repeated for the reasons of record. Applicant's arguments filed 7-8-02 have been fully considered but they are not persuasive.

Applicants argue that Official action mailed 8-29-01 does not offer explanation why the claimed method of infusing a rAAV vector expressing various gene product, such as anti-sense RNA, contractile protein, a growth factor, an angiogenic factor, a FGF, a VEGF etc., into a coronary artery or a coronary sinus to stably and efficiently transduce cardiomyocytes perfused through said artery or said sinus at various concentrations of rAAV vector. Applicants further argue that the Office has the initial burden to establish reasonable basis for the enablement rejection of the claimed invention (amendment, p. 4-7). This is not found persuasive because of

the reasons of record. As pointed out before, the claims are directed to gene therapy *in vivo* in light of the specification. Official action mailed 8-29-01 does indicate that the state of the prior art of gene therapy *in vivo* was not well developed and was unpredictable at the time of the invention, and does cite references Verma et al., and Eck et al. to support the unpredictability of gene transfer for gene therapy *in vivo*. In addition, the specification fails to provide adequate guidance and evidence for the correlation of a desired molecule encoded by various nucleic acid with a particular cardiovascular disease or condition. The specification also fails to provide adequate guidance and evidence whether the desired molecule would be expressed and be present in a sufficient amount at the targeted site such that said desired molecule could provide therapeutic effect for a particular cardiovascular disease or condition in a patient *in vivo*. Therefore, the Office has provided sufficient explanation for the enablement rejection of the claimed invention.

Applicants submitted Dr. Parmacek's declaration and argue that it was well known in the art to construct rAAV vector expressing various gene product as claimed and it is routine experimentation to construct said rAAV encoding a desired molecule, deliver it to an animal by infusion into a coronary artery or coronary sinus, and then transduce cardiomyocytes. Applicants further argue that Dr. Parmacek's declaration establishes the utility of the claimed method as for transducing non-human animal hearts *in vivo* to create animal models for human cardiovascular disease (amendment, p. 8-10). This is not found persuasive because of the reasons of record. A method of infusing a recombinant rAAV vector expressing a desired molecule into a coronary

artery or a coronary sinus so as to stably and efficiently transduce cardiomyocytes perfused through said artery or said sinus does not have specific and substantial utility. The working embodiment of the specification fails to provide a use for gene therapy *in vivo* and does not meet the requirement of 35 U.S. 101 because the lacZ embodiment is not taught to be useful in therapy, and the specification does not assert any specific or substantial utility for this specific embodiment nor does the evidence of record suggest a well-established utility for this specific embodiment. Dr. Parmacek's declaration is filed after the filing of the present application and the utility stated by Dr. Parmacek's declaration does not meet the 35 U.S.C. 101 utility requirement. Utility of a claimed invention must be provided at the time of filing not after the filing of an application.

Since the specification states "The ability to stably and efficiently program recombinant gene expression in cardiomyocytes facilitates gene therapy approaches for a variety of cardiovascular disease and conditions" and "The present invention is directed to a method of treating a cardiovascular condition by infusing an rAAV vector into a coronary artery or a coronary sinus for a time and in an amount sufficient to stably efficient transduce the cardiomyocytes perfused to the artery or sinus" (see specification, page 1, 3), the claims read on *in vivo* **gene therapy** for a variety of cardiovascular diseases and conditions in light of the specification.

As discussed above, the state of the prior art of gene therapy *in vivo* was not well developed and was unpredictable at the time of the invention as supported by Verma et al., and

Eck et al. Gene therapy *in vivo* using a rAAV vector expressing various gene product, such as anti-sense RNA, contractile protein, a growth factor, an angiogenic factor, a FGF, a VEGF etc., to treat cardiovascular diseases needs to considered separately because different gene products has different biological functions and pathologies of different cardiovascular diseases differ. Doses, schedules, responsive variables, required level and stability of gene expression, and criteria of success all depend on the gene used and the particular cardiovascular disease targeted. The specification fails to provide adequate guidance and evidence for the correlation of a desired molecule encoded by various nucleic acid with a particular cardiovascular disease or condition. The specification also fails to provide adequate guidance and evidence whether the desired molecule would be expressed and be present in a sufficient amount at the targeted site such that said desired molecule could provide therapeutic effect for a particular cardiovascular disease or condition in a patient *in vivo*. Thus, one skilled in the art would require undue experimentation to practice the invention claimed.

Applicants argue that examiner ignores the claimed subject matter and base enablement rejections on unclaimed subject matter, and the claimed invention has utility and is enabled as supported by Dr. Parmacek's declaration (amendment, p. 10-11). This is not found persuasive because of reasons of record and the reasons set forth above.

Conclusion

No claim is allowed.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Scott Priebe can be reached on (703) 308-7310. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Shin-Lin Chen, Ph.D.